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REVIEW

WILEY

Meta-analysis on the efficacy of psychological treatments for anorexia nervosa

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Abstract

Objective: This meta-analysis examines the efficacy of recently developed psychological treatments for anorexia nervosa, compared with control condition. Outcome criteria are weight gain, eating disorder pathology, and quality of life.

Method: Twelve thousand nine hundred ninety-seven abstracts, published between 1980 and 2017, were retrieved. End-of-treatment data from 1,279 participants, from 15 of 17 eligible studies, were used to calculate pooled-effect sizes (Hedges' g) for outcome using random-effects model. Subgroup analyses were used to explore the influence of various patient and study characteristics.

Results: No significant differences between psychological treatment and controls were found on weight gain, $g = 0.07$, 95% CI [−0.09, 0.23], eating disorder pathology, $g = 0.06$, 95% CI [−0.10, 0.21], and quality of life, $g = -0.11$, 95% CI [−0.36, 0.15]. Studies including only patients over 18 years of age were more effective on weight gain than studies including adolescents as well. High-quality studies and studies with reported therapist training had larger effects on weight gain and quality of life compared with low-quality studies and studies without reported training.

Conclusions: Despite progress in the development of specialized treatments, the efficacy of psychological treatment over an active control condition could not be established. Outcomes, however, are obscured by low-quality and heterogeneous studies.

KEYWORDS

anorexia nervosa, control condition, efficacy, meta-analysis, psychological treatment

1 | INTRODUCTION

Anorexia nervosa is a mental disorder with a poor prognosis (Galsworthy-Francis & Allan, 2014) and significant impact on the psychological and physical well-being of affected individuals (Hay et al., 2014). Anorexia nervosa has one of the highest mortality rates of all mental disorders (American Psychiatric Association, 2006). The American Psychiatric Association DSM-5 diagnostic criteria for anorexia (American Psychiatric Association, 2013) include self-imposed or maintained weight loss such that the person is underweight (for age and height) and associated over-evaluation of (the control of) shape and weight.

Elske van den Berga and Laura Houtzager contributed equally to this work.

Although there is a growing body of evidence that supports the efficacy of family treatment for adolescents and children, (Hay et al., 2014; NICE, 2017), there is a lack of high-quality evidence to guide the clinician in the treatment of adults who have anorexia nervosa. Specialized psychological treatments have not proven to be more effective than routine treatment control conditions (Fairburn, 2005). When comparing individual psychological therapies with each other, no specific treatment is consistently superior to any other specific approach (Hay, Claudino, Touyz, & Abd Elbaky, 2015).

Recent guidelines recommend that anorexia nervosa programmes should focus on engaging the patient, on nutritional and physical rehabilitation in order to regain weight and on provision of structured psychological treatment. In addition, treatment outcome should aim at supporting quality of life (QoL) changes, needed for improvement or recovery (NICE, 2017).

Although evidence is yet insufficient to support outpatient versus inpatient programmes, the treatment of anorexia nervosa has moved clinically from long-term inpatient programmes with outpatient follow-up to a more common model of individual outpatient treatment with hospital backup (Hay et al., 2015).

Methodologically robust studies are small in number and inconclusive, meaning that conflicting results are common in anorexia nervosa literature (Hay et al., 2014). In less recent randomized controlled trials (RCTs), sample sizes were inappropriate small, treatment outcomes were addressed in varied ways, and different treatments were employed within the same setting (Fairburn, 2005).

With the increase of recent RCTs run with newly developed psychological treatments and significantly larger sample sizes (Byrne et al., 2017), examining the effects by conducting an up-to-date meta-analysis including the most recent studies is sensible. This meta-analysis, in contrast to other recent meta-analyses (Murray, Quintana, Loeb, Griffiths, & Le Grange, 2018; Zeeck et al., 2018) includes end-of-treatment outcome measures on weight gain, eating disorder pathology, and on QoL. In addition, this study includes a 2017 large RCT (Byrne, 2017). Whereas other meta-analyses included RCTs on various nonpsychological treatment modalities (Murray et al., 2018), or studies comparing two psychological treatment conditions (Zeeck et al., 2018), this study examines the effects of psychological treatments versus a control condition for patients with anorexia nervosa from 12 years and older. This present study provides an up-to-date overview and is an addition to the available body of evidence regarding psychological treatment for anorexia nervosa.

Highlights

- No significant differences between psychological treatment and control condition were found on weight gain, on eating disorder pathology, and on quality of life.
- Studies including only patients over 18 years of age were more effective on weight gain than studies including adolescents as well.
- High-quality studies and studies with reported therapist training had larger effects on weight gain and quality of life compared with lower quality studies and studies without reported training.

2 | METHOD

Appendix A provides an overview of the extent to which this study was conducted in accordance to the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols guidelines (Moher et al., 2015).

2.1 | Selection procedure

For this meta-analysis, a systematic extensive electronic database literature search (from 1980 to 2017) for RCTs was conducted in the following databases: PubMed, PsycINFO, Embase, and Cochrane Library combining index and free terms of anorexia nervosa and psychological treatments (see Appendix B for an example of PubMed search string). Articles were also found via hand searches of reference lists by the first authors. The World Health Organization's International Clinical Trials Registry was searched for unpublished studies.

2.2 | Study selection

RCTs written in English or Dutch, published in peer-reviewed journals, were included in this meta-analysis if (a) a psychological treatment was compared with a control condition, (b) the psychological treatment consisted of at least some face to face verbal contacts, and (c) the study reported on patient groups diagnosed with anorexia nervosa and included patients 12 years of age or above. Studies or arms were excluded if insufficient statistics were available to calculate effect sizes.

Psychological treatments could include psychodynamic or psychoanalytic therapy, cognitive (behavioural) therapy, interpersonal therapy, family therapy, social

skills training, motivational interviewing, and combinations of the above. Control conditions to be included could be treatment as usual (TAU) among which are dietary advice and psychoeducational interventions and placebo conditions. The non-specific treatment modality Specialist Supportive Clinical Management (SSCM) is regarded as a control condition, although recent guidelines consider SSCM as a psychological treatment (NICE, 2017). Treatment and control conditions could be individually or group based, inpatient as well as outpatient settings were included. During the screening phases, the references were independently rated by three researchers (LH, EB, and GK). Discrepancies were resolved by consensus, and if needed, a senior reviewer was consulted (JD).

2.3 | Risk of bias

The quality of the studies was assessed using The Cochrane Collaboration's tool for assessing risk of bias in randomized trials (Higgins et al., 2011). The following domains on study and/or outcome level were independently assessed for each study by two researchers (EB and ID): sequence generation, allocation concealment, incomplete data, and selective outcome reporting. Assessing incomplete data included screening using intention-to-treat data. For each domain of potential bias, a value was given: "0" indicating low risk of bias, "2" indicating high risk, and "1" indicating lack of sufficient information for a value to be given. For each study, a global risk of bias score was computed by adding up the values of all domains. Studies with a very low risk of bias (i.e., no potential bias at all domains) were considered high-quality studies. Discrepancies were resolved by consensus within the review team, and if needed, a senior reviewer was consulted (EK).

2.4 | Outcomes

Meta-analyses were performed at post-treatment on intention-to-treat data. Primary outcome in this meta-analysis was weight gain. Weight gain could be measured in terms of kilogrammes (kg), body mass index (BMI: body weight in kg divided by height in m squared; kg/m^2), ideal body weight, adjusted body weight, mean matched population weight (expressed as the percentage of the average weight for age, height, and sex), or as a percentage of body fat. Eating disorder pathology was measured by a structured interview or a patient-reported measure, providing either a global score or separate scores for different domains. A measure of QoL was defined as any patient-reported measure assessing perceived QoL or social impairment due to eating disorder pathology. With regard to variables related to patient characteristics at baseline (BMI, onset age, and duration of illness), an average of the treatment and control condition for each arm was used.

2.5 | Statistical analysis

For each comparison between psychological treatment and control condition, we calculated the pooled-effect sizes (Hedges' *g*; weighted by inverse variance) for the primary and secondary outcomes. Effect sizes were calculated by subtracting the mean score at posttest of the psychological treatment group from the mean score of the control group and dividing the result by the pooled weighted standard deviations of the two groups. Effect sizes of 0–0.32 are considered to be small, whereas effect sizes of 0.33–0.55 are moderate, and effect sizes of 0.56–1.2 are large (Lipsey & Wilson, 1993). When means and standard deviations were not reported, we used other statistics (*p* value) to compute the effect size (Dare, Eisler, Russell, Treasure, & Dodge, 2001). As weight is assessed in various ways (see Appendix C), we reported a combined effect size. To explore whether this influenced the results, we also performed the meta-analyses including only BMI or kg.

With regard to our secondary outcome measures, we calculated pooled mean effect sizes, using the random effects model in the Comprehensive Meta-Analysis (CMA) software package (version 3; Borenstein & Rothstein, 2009). We also calculated the I^2 statistic, where a value of 0% indicates that there is no observed heterogeneity, 50% determines a moderate heterogeneity and 75% a high heterogeneity (Higgins, Thompson, Deeks, & Altman, 2003). The 95% confidence intervals around the I^2 was calculated using the non-central χ^2-based approach within the *heterogi* module for Stata (release 15; StataCorp., 2017). Potential publication bias was examined according to Duval and Tweedie's trim and fill procedure (Duval & Tweedie, 2000) using Comprehensive Meta-Analysis, which calculates an adjusted effect size taking into account missing studies. The symmetry of the funnel plots were tested using the Begg and Mazumdar rank correlation test (Begg & Mazumdar, 1994) and Egger's test (Egger, Davey Smith, Schneider, & Minder, 1997).

In this meta-analysis, five studies were included in which two psychological treatments were compared with the same control group (Byrne et al., 2017; Dare et al., 2001; Gowers et al., 2007; McIntosh et al., 2005; Zipfel et al., 2014), thus resulting in multiple

comparisons in the same analysis. Because those comparisons are not independent from each other, this may have resulted in an artificial reduction of heterogeneity and may have influenced the pooled effect size. We therefore performed a sensitivity analysis by including the largest effect size and smallest effect size for each of these studies separately. Sensitivity analyses were conducted on low risk of bias studies and on outpatient studies.

Subgroup analyses were used to explore the influence of various patient and study characteristics. We performed subgroup analyses when at least three studies were available per subgroup condition. Subgroup analyses were performed using the mixed effects model, which pools studies within subgroups with the random effects model and tests for significant differences between subgroups with the fixed effects model. Given the modest evidence for family therapy for younger anorexia nervosa patients, living with their family and an illness duration of less than three years (Hay et al., 2014) subgroup analyses were performed on studies including patients under 18 and on studies including family therapy. Given the efficiency of the control condition SSCM (NICE, 2017), subgroup analyses were performed on studies including SSCM. Additional subgroup analyses for the study characteristics baseline BMI, age of illness onset, duration of illness, therapy setting, number of treatment sessions, availability of treatment manual, and training of the therapists were exploratory.

Finally, we conducted meta-regression analyses using the mixed effects model, to assess whether the continuous variable year of publication predicted the effect sizes, indicated by a z value and an associated p value.

2.5.1 | Power calculation

We conducted a power calculation according to the procedures described by Borenstein, Hedges, and Rothstein (2009), to examine how many studies would have to be included in order to have sufficient statistical power to identify significant effects. We estimated the number of studies needed to identify an effect size of 0.3. The power calculation indicated at least 20 studies with a mean sample size of 30 (15 participants per condition) had to be included, for being able to detect an effect size of $d = .30$ (conservatively assuming a medium level of between-study variance, $\tau 2$, a statistical power of .80, and a significance level of $\alpha = .05$). Alternatively, we would need 15 studies with 40 participants each or 14 studies with 50 participants to detect an effect size of $d = .30$.

3 | RESULTS

The search yielded 12.997 results out of which a total of potential 169 RCTs remained for a subsequent full-text screening. At the latest update, it was decided to exclude RCTs published before 1980. No unpublished eligible RCTs were found. Finally, 17 studies were included in this meta-analysis (see PRISMA flow chart, Figure 1).

3.1 | Study characteristics

The 17 RCTs included a total of 1,279 participants: 761 in the psychological treatment conditions and 518 in the control treatment conditions (see Appendix C). Some studies reported on multiple psychological treatment conditions versus one control condition, resulting in a total of 24 arms. Most studies included adult patients ($n = 9$), three reported on adolescents, and five reported on both adolescents and adults. The number of patients in the experimental conditions ranged from 10 to 80 per study. Mean pretreatment BMI ranged from 15.0 to 18.1.

The majority of the treatment conditions for adults reported on cognitive (behaviour) therapy ($n = 5$), Maudsley Model of Anorexia Nervosa Treatment for Adults ($n = 3$), or cognitive analytical psychotherapy or focal psychodynamic therapy ($n = 4$). In studies in which only adolescents were treated, all treatment conditions included family interventions ($n = 3$). The majority of the control conditions was defined as TAU ($n = 6$) or SSCM ($n = 5$).

Three of the 17 studies were inpatient studies, although hospitalization was offered to a minority of patients in several outpatient studies. In one study, both an inpatient and an outpatient treatments were compared with TAU (Gowers et al., 2007). Besides the family therapy conditions, all conditions but one (Pillay & Crisp, 1981) were individually based treatments. The offered outpatient treatment doses ranged from four sessions (Motivational Interviewing; Wade, Frayne, Edwards, Robertson, & Gilchrist, 2009) to a little over 40 sessions (Cognitive Behavioral Therapy-Enhanced; Byrne et al., 2017, and Focal Psychodynamic Therapy; Zipfel et al., 2014). The mean number of outpatient sessions was 23.2 (range 0–58.3), and dropout rates per arm ranged from 7% (Hall & Crisp, 1987) to 100% (Serfaty, Turkington, Heap, Ledsham, & Jolley, 1999).

Six studies were assessed as having a low risk of bias based on the Cochrane domains (Higgins et al., 2011), meaning that 35% of the included studies are regarded high-quality studies. A high risk of bias with regard to the domain *incomplete data* was the most commonly found risk of bias ($n = 4$). With regard to *allocation*

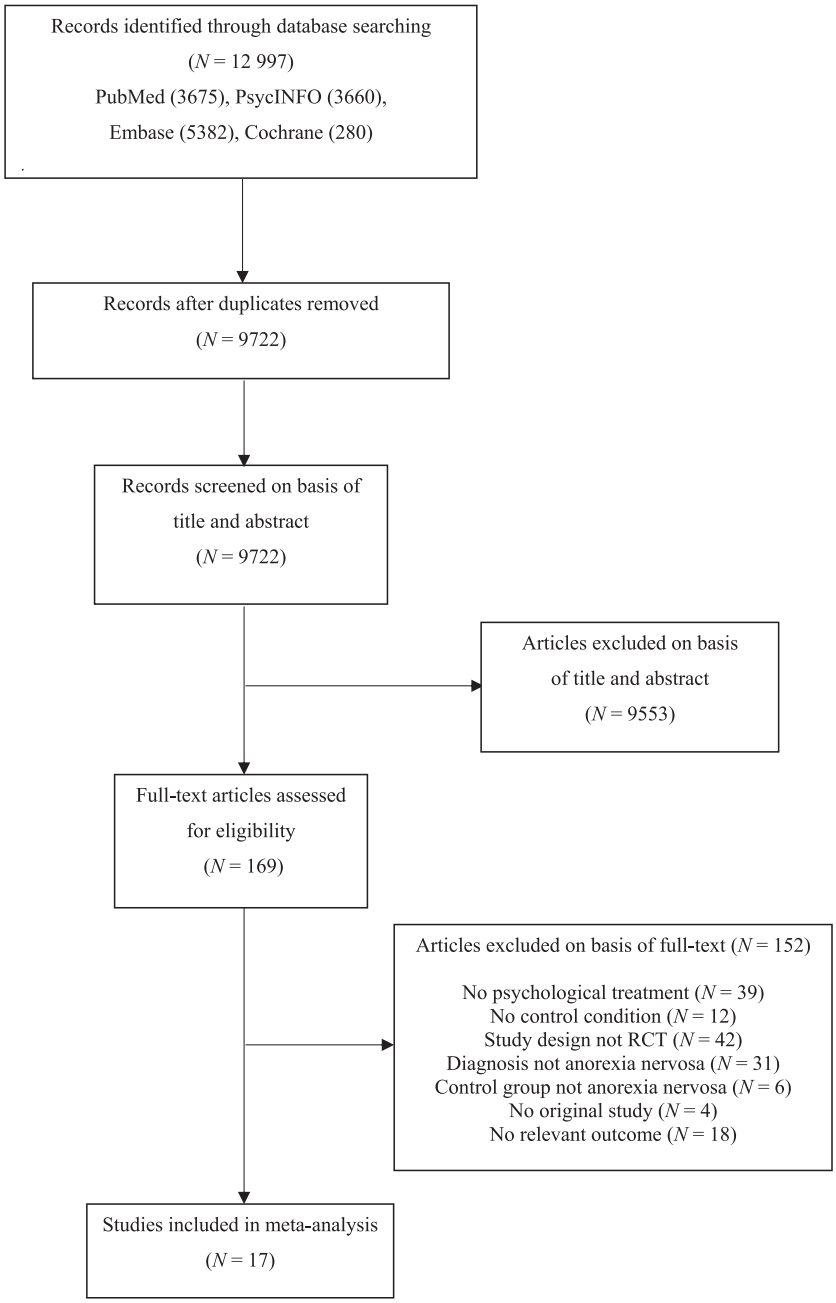


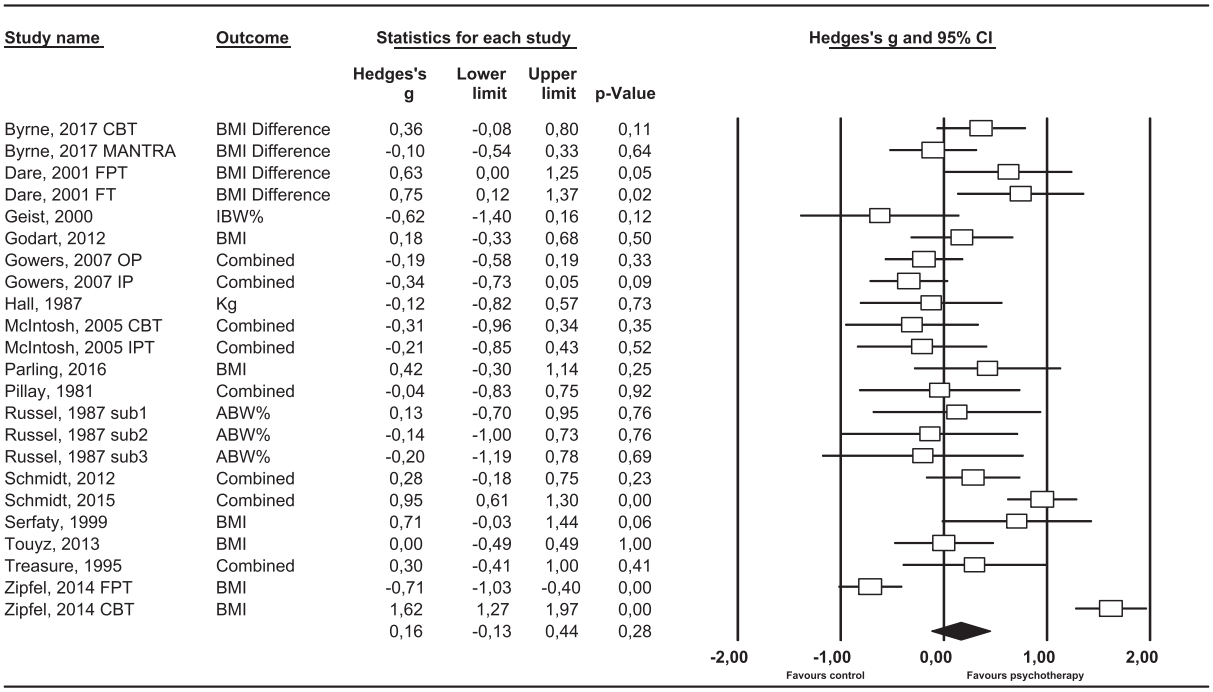
FIGURE 1 Preferred reporting items for systematic review and meta-analysis flow chart of the study selection process

concealment, this domain was unclear in seven studies and was in one study found to be a high risk of bias. All relevant study characteristics can be found in Appendix C.

3.2 | Weight gain

Twenty comparisons were included in the meta-analysis of weight gain (Figure 2). The pooled effect size indicating the difference between psychological treatment and control condition on weight gain at post-treatment was not significant, $g = 0.07$, 95% CI [−0.09, 0.23]. Similarly, no significant differences were found when the effects were examined for BMI and kg separately (Table 1). Including all 23 comparisons from 16 studies resulted in a very high between-study heterogeneity, $I^2 = 85$, 95% CI [78, 89]. Removing three outlier arms lowered heterogeneity to $I^2 = 30$, 95% CI [0, 59]. No indication for publication bias was found.

Sensitivity analysis including only the largest effect size of each study resulted in an overall effect size of $g = 0.10$, 95% CI [−0.09, 0.28]. When only the smallest effect size was included, the pooled effect size was $g = 0.06$, 95% CI [−0.10, 0.21]. Including only high-quality studies in a sensitivity analysis did not result in a significant difference between treatment and control conditions.



ABW = Average body weight; BMI = Body Mass Index; CBT = Cognitive Behavior Therapy; FPT = Focal psychodynamic therapy; FT = Family therapy; IBW = Ideal body weight; IP = inpatient; IPT = Interpersonal Therapy; MANTRA = Maudsley Model of Anorexia Nervosa Treatment for Adults; OP = outpatient; sub = subgroup

FIGURE 2 Standardized mean differences of psychological treatments for anorexia nervosa compared with control conditions on weight gain

Subgroup analyses showed that studies including patients of 18 years of age had a significantly higher effect size, $g = 0.23$, 95% CI [0.06, 0.40], than studies including patients under 18, $g = -0.18$, 95% CI [−0.41, 0.6], $p = .006$. High-quality studies differed significantly, $g = 0.27$, 95% CI [0.02, 0.52], from lower quality studies, $g = -0.08$, 95% CI [−0.24, 0.09], $p = .025$, with regard to the effect on weight gain.

Meta-regression analysis showed that publication year was not significantly associated with effect on weight gain, $b = 0.002$, 95% CI [−0.01, 0.02], $p = .813$.

3.3 | Eating disorder pathology

Thirteen comparisons were included in the meta-analysis of eating disorder pathology. No significant difference between psychological treatment and control treatment on eating disorder pathology was found, $g = 0.06$, 95% CI [−0.10, 0.21]. Examining the effects for BMI and kg separately does not lead to a different finding. A very high between-study heterogeneity was detected including all 16 comparisons, $I^2 = 87$, 95% CI [80, 91]. After removing three outliers, heterogeneity lowered, $I^2 = 17$, 95% CI [0, 56] (Table 2). Examining potential publication bias using Duvall and Tweedie's trim and fill procedure resulted in $g = 0.10$, 95% CI [−0.07, 0.26], with one study imputed. Testing the symmetry of the funnel plot using the Begg and Mazumbar's test (Kendall's $T = 0.064$, $p = .760$) and Egger's test ($T = 0.358$, $df = 11$, $p = .727$) did not reveal significant publication bias.

Sensitivity analyses including only the largest or smallest effect size of each study, including only high-quality studies, or including only outpatient studies, did not result in significant differences between treatment and control conditions. Neither when the effects were examined for Eating Disorder Examination-Interview and Eating Disorder Inventory separately. Finally, a series of subgroup analyses were conducted, but none of the included moderators was significantly associated with eating disorder pathology. The meta-regression analysis showed that publication year was not significantly associated with the effect on eating disorder pathology, $b = 0.002$, 95% CI [−0.04, 0.02], $p = .626$.

3.4 | Quality of life

Nine comparisons were included in the meta-analysis of the effect of psychological treatment on QoL, and no significant differences were found on QoL, $g = 0.11$, 95% CI [−0.36, 0.15]. Including all ten comparisons led to a high

TABLE 1 Weight gain: Effect sizes in meta-analysis of studies comparing psychological treatment with a control condition

		Effect size		Heterogeneity		
Comparison	**Number of comparisons**	***g***	**95% CI**	I^2	**95% CI**	***p***
Total sample						
All studies	23	0.16	[−0.13, 0.44]	85	[78, 89]	
Adjusted values	29	0.35	[0.08, 0.63]		—	
One effect size per study (highest)	18	0.25	[−0.06, 0.56]	82	[72, 88]	
One effect size per study (lowest)	18	0.07	[−0.18, 0.33]	73	[58, 83]	
Only outpatient studies	20	0.23	[−0.08, 0.54]	86	[79, 90]	
Only high quality studies	9	0.42	[−0.12, 0.95]	92	[89, 96]	
Body Mass Index	13	0.21	[−0.23, 0.64]	91	[87, 94]	
Kg	7	0.23	[−0.13, 0.59]	63	[17, 84]	
Sample without outliers						
All studies	20	0.07	[−0.09, 0.23]	30	[0, 59]	
Adjusted values	0	—	—		—	
One effect size per study (highest)	16	0.10	[−0.09, 0.28]	28	[0, 61]	
One effect size per study (lowest)	16	0.06	[−0.10, 0.21]	3	[0, 54]	
Only outpatient studies	17	0.13	[−0.02, 0.29]	16	[0, 53]	
Only high-quality studies	6	0.27	[0.02, 0.52]	35	[0, 74]	
Body Mass Index	10	0.00	[−0.19, 0.20]	23	[0, 63]	
Kg	6	0.11	[−0.17, 0.39]	14	[0, 78]	
Subgroup analyses						
Age						
<18 years	5	−0.18	[−0.41, 0.06]	8	[0, 81]	.006
≥ 18 years	13	0.23	[0.06, 0.40]	4	[0, 58]	
Onset age						
<18 years	6	0.02	[−0.27, 0.30]	0	[0, 75]	.055
≥18 years	5	0.41	[0.13, 0.69]	0	[0, 79]	
Duration of illness						
<24 months	4	−0.14	[−0.37, 0.09]	0	[0, 85]	.054
24–48 months	5	0.14	[−0.17, 0.45]	27	[0, 71]	
>48 months	5	0.31	[0.01, 0.62]	27	[0, 71]	
Type therapy						
CBT-enhanced	3	0.07	[−0.29, 0.44]	34	[0, 78	.841
Family therapy	7	0.03	[−.27, 0.34]	36	[0, 73]	
Other	9	0.14	[−0.08, 0.37]	28	[0, 67]	
Format therapy						
Individual	10	0.18	[−0.02, 0.38]	19	[0, 60]	.104
Other	10	−0.07	[−0.29, 0.16]	25	[0, 64]	
N sessions						
<15	6	0.01	[−0.40, 0.42]	40	[0, 76]	.383
15–25	7	0.25	[−0.03, 0.53]	25	[0, 67]	
>25	5	0.00	[−0.25, 0.25]	36	[0, 76]	

(Continues)

TABLE 1 (Continued)

Comparison	Number of comparisons	Effect size		Heterogeneity		
		g	95% CI	I^2	95% CI	*p*
Control condition						
Specialist supportive clinical management	6	0.06	[−0.15, 0.26]	4	[0, 76]	.702
Treatment as usual	11	0.14	[−0.11, 0.39]	46	[0, 73]	
Other	3	−0.10	[−0.63, 0.43]	33	[0, 93]	
Risk of bias						
High quality	6	0.27	[0.02, 0.52]	35	[0, 74]	.025
Other studies	14	−0.08	[−0.24, 0.09]	2	[0, 56]	
Manual reported?						
Yes	9	0.10	[−0.14, 0.34]	39	[0, 72]	.714
No	11	0.04	[−0.18, 0.26]	28	[0, 64]	
Training reported?						
Yes	11	0.10	[−0.11, 0.30]	30	[0, 65]	.696
No	9	0.03	[−0.23, 0.29]	37	[0, 71]	
Meta-regression						
		B	95% CI	*SE*		*p*
Year of publication		0.002	[−0.01, 0.02]	0.01		.813

heterogeneity, $I^2 = 71$, 95% CI [46, 85], so one outlier was removed, lowering heterogeneity to $I^2 = 48$, 95% CI [0, 76] (Table 3). No indication for publication bias was found.

Sensitivity analyses including only the largest or smallest effect size of each study, including only high-quality studies, or including only outpatient studies did not result in significant differences between treatment and control condition. Neither when the effects were examined for the Clinical Impairment Assessment separately.

Subgroup analysis showed that the effect of high-quality studies on Qol was significantly different, $g = 0.10$, 95% CI [−0.17, 0.38], compared with lower quality studies, $g = -0.35$, 95% CI [−0.70, 0.01], $p = .041$. Furthermore, a significant difference on QoL was found between studies in which therapist training was reported, $g = 0.10$, 95% CI [−0.17, 0.38], compared with studies in which training was not reported, $g = -0.35$, 95% CI [−0.70, 0.01], $p = .042$.

Meta-regression showed that publication year was not significantly associated with the effects on QoL, $b = 0.009$, 95% CI [−0.02, 0.04], $p = .534$.

4 | DISCUSSION

In this meta-analysis, the efficacy of psychological treatments for anorexia nervosa compared with a control condition was examined. The results suggest that with regard to weight gain, eating disorder pathology, and QoL, no differences between psychological treatment and control condition are found. Studies including only patients over 18 years of age were more effective on weight gain than studies including adolescents as well. High-quality studies (i.e., studies that are methodologically robust) differed significantly from low-quality studies with regard to weight gain. In addition, with regard to QoL, high-quality studies and studies in which therapist training was reported differed significantly from low-quality studies and studies without reported training. However, including only high-quality studies in the meta-analyses did not establish a significant difference between psychological and control conditions.

The main finding of not being able to establish differences between psychological treatment and control conditions with regard to weight gain and/or eating disorder pathology is in line with previous studies (Hay, Claudino, Smith, et al., 2015; Zeeck et al., 2018). Adding recent, large RCTs, as we did in this meta-analysis, did not result in a different finding. The recent meta-analysis of Murray (Murray et al., 2018) found that specialist treatments (not just psychological treatments) showed a significant treatment effect over control conditions with regard to weight-based symptoms improvement at end-of-treatment, although at follow-up, this difference did not last. The results suggest that the field still lacks psychological interventions of enough strength for added value to be detected.

TABLE 2 Eating disorder pathology: Effect sizes in meta-analysis of studies comparing psychological treatment with a control condition

Comparison	Number of comparisons	Effect size		Heterogeneity		
		g	95% CI	I^2	95% CI	*p*
Total sample						
All studies	16	0.30	[−0.03, 0.62]	87	[80, 91]	
Adjusted values	20	0.45	[0.16, 0.74]		—	
One effect size per study (highest)	12	0.34	[−0.09, 0.77]	89	[82, 93]	
One effect size per study (lowest)	12	0.29	[0.03, 0.55]	70	[45, 83]	
Only outpatient studies	14	0.32	[−0.04, 0.68]	88	[81, 92]	
Only high-quality studies	7	0.63	[0.09, 1.17]	92	[86, 95]	
Eating Disorder Examination-Interview—Global	8	0.18	[−0.25, 0.62]	84	[71, 92]	
Eating Disorder Inventory—Global	5	0.48	[0.05, 0.91]	84	[63, 93]	
Sample without outliers						
All studies	13	0.06	[−0.10, 0.21]	17	[0, 56]	
Adjusted values	14	0.10	[−0.07, 0.26]		—	
One effect size per study (highest)	10	0.10	[−0.12, 0.31]	35	[0, 69]	
One effect size per study (lowest)	10	0.14	[−0.05, 0.32]	14	[0, 55]	
Only OP studies	11	0.06	[−0.13, 0.25]	28	[0, 65]	
Only high-quality studies	4	0.17	[−0.28, 0.62]	74	[28, 91]	
Eating Disorder Examination—Global	7	0.04	[−0.28, 0.36]	63	[15, 84]	
Eating Disorder Inventory	10	0.07	[−0.14, 0.29]	47	[0, 74]	
Subgroup analyses						
Age						
<18 years	4	−0.01	[−0.24, 0.23	0	[0, 85]	.491
≥18 years	7	0.13	[−0.17, 0.42]	53	[0, 80]	
Duration of illness						
<24 months	3	−0.03	[−0.28, 0.21]	0	[0, 90]	.417
>24 months	5	0.15	[−0.22, 0.51]	66	[12, 87]	
Type therapy						
CBT-enhanced	3	−0.01	[−0.41, 0.39]	44	[0, 83]	.869
Family therapy	3	0.02	[−0.27, 0.30]	0	[0, 90]	
Other	7	0.10	[−0.16, 0.36]	39	[0, 74]	
Format therapy						
Individual	9	0.09	[−0.15, 0.33]	41	[0, 73]	.593
Other	4	−0.01	[−0.24, 0.23]	0	[0, 85]	
N sessions						
<25	7	0.15	[−0.13, 0.43]	35	[0, 72]	.344
>25	4	−0.03	[−0.28, 0.22]	17	[0, 87]	
Control condition						
Specialist Supportive Clinical Management	6	0.10	[−0.23, 0.43]	60	[3, 84]	.504
Treatment as usual	5	−0.04	[−0.25, 0.18[	0	[0, 79]	
Risk of bias						
High quality	4	0.17	[−0.28, 0.62]	74	[28, 91]	.474

(Continues)

TABLE 2 (Continued)

Comparison	Number of comparisons	Effect size		Heterogeneity		
		g	95% CI	I^2	95% CI	*p*
Other studies	9	−0.01	[−0.19, 0.17]	0	[0, 65]	
Manual reported?						
Yes	9	0.09	[−0.15, .32]	40	[0, 72]	.542
No	4	−0.01	[−0.25, 0.22]	0	[0, 85]	
Training reported?						
Yes	6	0.11	[−0.18, 0.41]	59	[0, 83]	.527
No	7	−0.01	[−0.23, 0.21]	0	[0, 71]	
Meta-regression						
		B	95% CI	*SE*		*p*
Year of publication		−0.002	[−0.04, 0.02]	.02		.626

At the same time, it seems that low-quality studies obscure the effects of psychological treatment. The finding that high-quality studies differ significantly from low-quality studies with regard to weight gain and QoL suggests that psychological interventions can have additional benefits over and above control treatment.

In addition, the lack of difference between psychological and control condition may also be related to the fact that included studies are heterogeneous; even the recent large, methodologically sound RCTs are heterogeneous and show contradictory findings. Furthermore, the lack of difference can possibly be explained by the nature of the control conditions. The control conditions in this meta-analysis consisted of multimodal interventions in line with recommended core elements for anorexia nervosa treatment, such as engaging the patient, nutritional and physical rehabilitation, and structured psychological interventions (Hay, Claudino, Smith, et al., 2015). By using such plausible active control conditions, it is hard to distinguish the additional benefits of psychological treatment for anorexia nervosa.

In recent guidelines, SSCM is one of the psychological treatments to be considered (NICE, 2017). In this meta-analysis, SSCM is regarded a control treatment, in line with the original design in all RCTs but one (Touyz et al., 2013) including SSCM. Subgroups analyses did not show a difference in effect size on weight gain, eating disorder pathology, or Qol between SSCM and other TAU conditions.

To our knowledge, there are no previous studies in line with our finding that for patients over 18, a larger effect on weight gain is found; former theorizing did postulate that treatment targeted at adolescents was more efficacious (Murray et al., 2018). In the recent meta-analysis of Murray et al. (2018), age did not moderate treatment outcome. Zeeck et al. (2018) stated that psychotherapeutic interventions seemed to be more effective in terms of weight gain for adolescents. In both studies, however, it is unclear whether "adolescent" was strictly defined as being under 18. With the small number of included high-quality studies, it is of interest, when more high-quality studies are becoming available for conducting meta-analyses, whether our finding can be replicated.

The finding that training therapists lead to better outcome, at least on QoL, matches earlier studies that proper training is related to improved outcome (Gyani, Shafran, Layard, & Clark, 2013). Literature suggests that manualized based approaches led by a specialist (i.e., trained) therapist show the most promising evidence base (Hay et al., 2014).

4.1 | Limitations

Our meta-analysis has several limitations, and therefore, the results should be interpreted with caution. Due to the high statistical heterogeneity, we had to exclude two outlier studies (Schmidt et al., 2015; Zipfel et al., 2014) from all further analyses. Schmidt et al. (2015) compared the Maudsley Model of Anorexia Nervosa Treatment for Adults with SSCM. In the study from Zipfel et al. (2014), focal psychodynamic therapy was compared with enhanced cognitive behaviour therapy and with a broad optimized treatment-as-usual condition. In both studies, no significant differences between the conditions were found. The treatment and control arms differed greatly from each other, and the five comparisons showed outcomes in different directions; with regard to weight gain, in the Zipfel study, one treatment arm was more effective than control, and one treatment arm was less effective. On eating disorder pathology, both treatment conditions

TABLE 3 Quality of life: Effect sizes in meta-analysis of studies comparing psychological treatment with a control condition

Comparison	Number of comparisons	Effect size		Heterogeneity		
		g	95% CI	I^2	95% CI	*p*
Total sample						
All studies	10	−0.02	[−0.33, 0.28]	71	[46, 85]	
Adjusted values	13	0.18	[−0.13, 0.49]		—	
One effect size per study (highest)	8	0.04	[−0.31, 0.39]	73	[45, 87]	
One effect size per study (lowest)	8	0.09	[−0.22, 0.41]	66	[29, 84]	
Only outpatient studies	9	−0.02	[−0.35, 0.31]	74	[51, 87]	
Only high-quality studies	5	0.25	[−0.10, 0.59]	70	[23, 88]	
Clinical impairment assessment	4	0.29	[−0.13, 0.70]	75	[32, 91]	
Sample without outliers						
All studies	9	−0.11	[−0.36, 0.15]	48	[0, 76]	
Adjusted values	0	—	—		—	
One effect size per study (highest)	7	−0.07	[−0.37, 0.24]	52	[0, 79]	
One effect size per study (lowest)	7	0.00	[−0.26, 0.25]	32	[0, 71]	
Only outpatient studies	8	−0.12	[−0.39, 0.16]	54	[0, 79]	
Only high-quality studies	4	0.10	[−0.17, 0.38]	31	[0, 75]	
Clinical impairment assessment	3	0.12	[−0.26, 0.50]	54	[0, 87]	
Subgroup analyses						
Type therapy						
CBT-enhanced	3	−0.17	[−0.51, 0.18	25	[0, 92]	.840
Other	5	−0.11	[−0.57, 0.35]	67	[14, 87]	
N sessions						
15–25	4	−0.29	[−0.98, 0.39]	79	[45, 92]	.471
>25	4	−0.02	[−0.26, 0.21]	0	[0, 85]	
Control condition						
Specialist supportive clinical management	6	−0.13	[−0.49, 0.23]	66	[20, 86]	.879
Other	3	−0.09	[−0.45, 0.28]	0	[0, 90]	
Risk of bias						
High quality	4	0.10	[−0.17, 0.38]	31	[0, 75]	.041
Other studies	5	−0.35	[−0.70, 0.01]	27	[0, 71]	
Manual reported?						
Yes	6	−0.18	[−0.57, 0.22]	67	[21, 86]	.533
No	3	−0.02	[−0.32, 0.28]	0	[0, 90]	
Training reported?						
Yes	4	0.10	[−0.17, 0.38]	31	[0, 75]	.042
No	5	−0.35	[−0.70, 0.01]	27	[0, 71]	
Meta-regression						
		B	95% CI	*SE*		*p*
Year of publication		0.009	[−0.02, 0.04]	.01		.534

were more effective than control. In the Schmidt 2015 study, the treatment condition did better than control with regard to both weight gain and eating disorder pathology. In both studies, none of the found differences were statistically significant. These studies are recent, large RCTs, and it is possible that their findings may be

closer to true effect size of psychological interventions. However, it was decided to exclude them because their presence influenced subsequent subgroup analyses, and thus, it could not be concluded whether subgroup differences were related to the particular subset of studies (e.g., high-quality trials) or due to the presence of these two outliers.

The finding of high heterogeneity can also be indicative of a large variety in included patient groups. In addition, the variety in used outcome measurements, probably assessing slightly different constructs, may have increased heterogeneity.

This large variety in measures led to a limited number of studies that could be included in the subgroup analyses. Because of these small sample sizes, we may have lacked adequate power to detect effect sizes.

In the included studies, both in the treatment and in control arms, a large variety of interventions is used. There are only few direct replications, and these replication studies have been done with different patient populations, leading to small subgroup samples.

Finally, in addition to previous mentioned risk of biases, in some studies, principal investigators were also responsible for the development of treatment interventions used in the RCT, so researcher allegiance cannot be excluded.

4.2 | Suggestions for further research

In general, by using meta-analysis, multiple trials showing non-significant or only minor benefits may result in a significant difference between products as the power of the individual studies is magnified. Alternatively, the significant benefit observed in a few trials may be outweighed by multiple trials showing no difference between products. Therefore, using individual patient data, meta-analyses, instead, might produce a better estimate of the pooled effect size.

Standardized outcome measures are essential in the assessments of the treatment effects and should preferable be chosen in line with other, high-quality RCTs. In addition, replication studies in which similar psychological interventions are replicated for homogenous patient groups may reduce heterogeneity.

4.3 | Implications

The finding that therapist training seems to be related to outcome is a reminder that proper training for staff is essential in order for being able to deliver the original treatment to its full potential.

4.4 | Conclusion

This meta-analysis shows that, despite progress in development of new psychological treatments, the efficacy of psychological treatment over control condition could not be established. Although no indication for publication bias was found, the number of low-quality studies and the high heterogeneity reduces the strength of the evidence. More high-quality, homogeneous data are needed for firm conclusions regarding the efficacy of psychological treatment for anorexia nervosa to be drawn.

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CONFLICT OF INTEREST

All authors declare they have no conflict of interest.

AUTHOR CONTIBUTIONS

Author Elske van den Berg contributed to study design, data acquisition, analysis plan, literature search, drafting of the manuscript and appendices, and final approval. Author Laura Houtzager contributed to study design, analysis plan, literature search, and drafting of the manuscript. Author Jasmijn de Vos contributed to study design, analysis plan, literature search, and drafting of the manuscript. Author Georgia Katsaragaki contributed to literature search and analysis plan. Author Eirini Karyotaki contributed to data acquisition, analysis plan, and final approval. Author Inge Daemen contributed to study design, data acquisition, analysis plan, and did the analysis, literature search, and drafting of the manuscript and appendices. Author Pim Cuijpers contributed to final approval. Author Jack Dekker contributed to study design and data acquisition and contributed to final approval. All authors approved the final version.

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APPENDIX A

PRISMA-P 2015 CHECKLIST

This checklist has been adapted for use with protocol submissions to *Systematic Reviews* from Table 3 in Moher D et al: Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews* 2015 **4**:1

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
ADMINISTRATIVE INFORMATION					
Title					
Identification	1a	Identify the report as a protocol of a systematic review	X	☐	Pg. 1, line 1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	☐	X	—
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	☐	X	—
Authors					
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	X	☐	Pg. 1, line 27–39
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	X	☐	Pg. 2, line 8–17

(Continued)

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	☐	X	—
Support					
Sources	5a	Indicate sources of financial or other support for the review	X	☐	Pg. 2, line 2–3
Sponsor	5b	Provide name for the review funder and/or sponsor	X	☐	Pg. 2, line 2–3
Role of sponsor/ funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	X	☐	Pg. 2, line 2–3
INTRODUCTION					
Rationale	6	Describe the rationale for the review in the context of what is already known	X	☐	Pg. 6, line 4–15
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	X	☐	Pg 6., line 4–15
METHODS					
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review	X	☐	Pg. 7, line 7–17
Information sources	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	X	☐	Pg. 6, line 23–25 – pg. 7, line 1–4
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	X	☐	Appendix B
STUDY RECORDS					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	X	☐	Pg. 8, line 14–24
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	X	☐	Pg. 7, line 21–23
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	X	☐	Pg. 6, line 23–25 – pg. 7, line 1–4
Data items	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	X	☐	Pg. 8, line 14–24 Pg. 10, line 7–18
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	X	☐	Pg. 8, line 14–24 Pg. 10, line 7–18
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	X	☐	Pg. 8, line 1–11
DATA					
Synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	X	☐	Pg. 8, line 14
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., I^2, Kendall's tau)	X	☐	Pg. 9, line 2–23
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	X	☐	Pg.10, line 7–21

(Continued)

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	☐	X	—
Meta-bias (es)	16	Specify any planned assessment of meta-bias (es; e.g., publication bias across studies, selective reporting within studies)	X	☐	Pg. 13, line 5Pg. 16, line 7–11Pg. 20, line 4–5
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	X	☐	Pg. 27, line 8–11

APPENDIX B

PUBMED SEARCH STRING

1. Eating disorder

(Eating Disorders [MH] OR "Eating Disorder"[All Fields] OR "Anorexia Nervosa"[MH] OR "Anorexia"[All Fields] OR "Bulimia Nervosa"[MH] OR "bulimia"[All Fields] OR "binge eating disorder"[All Fields] OR "BED"[All Fields] OR "eating disturbance"[All Fields] OR "disturbed eating"[All Fields] OR "disturbed eating behaviour"[All Fields] OR "binge eating"[All Fields] OR "binge-purge"[All Fields] OR "purging"[All Fields])

2. Therapy: Psychotherapy and/or pharmacotherapy

(Psychotherapy [MH] OR psychotherap*[All Fields] OR cbt[All Fields] OR "behavior therapies"[All Fields] OR "behavior therapy"[All Fields] OR "behavior therapeutic"[All Fields] OR "behavior therapeutical"[All Fields] OR "behavior therapeutics"[All Fields] OR "behavior therapeutist"[All Fields] OR "behavior therapeutists"[All Fields] OR "behavior treatment"[All Fields] OR "behavior treatments"[All Fields] OR "behaviors therapies"[All Fields] OR "behaviors therapy"[All Fields] OR "behaviors therapeutics"[All Fields] OR "behaviors therapeutic"[All Fields] OR "behaviors therapeutical"[All Fields] OR "behaviors therapeutist"[All Fields] OR "behaviors therapeutists"[All Fields] OR "behaviors treatment"[All Fields] OR "behaviors treatments"[All Fields] OR "behavioral therapies"[All Fields] OR "behavioral therapy"[All Fields] OR "behavioral therapeutics"[All Fields] OR "behavioral therapeutic"[All Fields] OR "behavioral therapeutical"[All Fields] OR "behavioral therapeutist"[All Fields] OR "behavioral therapeutists"[All Fields] OR "behavioral treatment"[All Fields] OR "behavioral treatments"[All Fields] OR "behaviour therapies"[All Fields] OR "behaviour therapy"[All Fields] OR "behaviour therapeutic"[All Fields] OR "behavior therapeutical"[All Fields] OR "behaviour therapeutics"[All Fields] OR "behavior therapeutist"[all Fields] OR "behavior therapeutists"[All Fields] OR "behaviour treatment"[All Fields] OR "behaviour treatments"[All Fields] OR "behaviours therapies"[All Fields] OR "behaviours therapy"[All Fields] OR "behaviours therapeutics"[All Fields] OR "behaviours therapeutic"[All Fields] OR "behaviours therapeutical"[All Fields] OR "behaviours therapeutist"[All Fields] OR "behaviours therapeutists"[All Fields] OR "behaviours treatment"[All Fields] OR "behaviours treatments"[All Fields] OR "behavioural therapies"[All Fields] OR "behavioural therapy"[All Fields] OR "behavioural therapeutics"[All Fields] OR "behavioural therapeutic"[All Fields] OR "behavioural therapeutical"[All Fields] OR "behavioural therapeutist"[All Fields] OR "behavioural therapeutists"[All Fields] OR "behavioural treatment"[All Fields] OR "behavioural treatments"[All Fields] OR "cognition therapies"[All Fields] OR "cognition therapie"[All Fields] OR "cognition therapy"[All Fields] OR "cognition therapeutical"[All Fields] OR "cognition therapeutic"[All Fields] OR "cognition therapeutics"[All Fields] OR "cognition therapeutist"[All Fields] OR "cognition therapeutists"[All Fields] OR "cognition treatment"[All Fields] OR "cognition treatments"[All Fields] OR psychodynamic[All Fields] OR Psychoanalysis[MH] OR psychoanalysis[All Fields] OR psychoanalytic*[All Fields] OR counselling[All Fields] OR counseling[All Fields] OR Counseling[MH] OR "problem-solving"[All Fields] OR mindfulness[All Fields] OR (acceptance[All Fields] AND commitment[All Fields]) OR "assertiveness training"[All Fields] OR "behavior activation"[All Fields] OR "behaviors activation"[All Fields] OR "behavioral activation"[All Fields] OR "cognitive therapies"[All Fields] OR "cognitive

therapy"[All Fields] OR "cognitive therapeutic"[All Fields] OR "cognitive therapeutics"[All Fields] OR "cognitive therapeutical"[All Fields] OR "cognitive therapeutist"[All Fields] OR "cognitive therapeutists"[All Fields] OR "cognitive treatment"[All Fields] OR "cognitive treatments"[All Fields] OR "cognitive restructuring"[All Fields] OR (("compassion-focused"[All Fields] OR "compassion-focussed"[All Fields]) OR "solution-focused therapies"[All Fields] OR "solution-focused therapy"[All Fields] OR "solution-focused therapeutic"[All Fields] OR "solution-focused therapeutics"[All Fields] OR "solution-focused therapeutical"[All Fields] OR "solution focused therapies"[All Fields] OR "solution focused therapy"[All Fields] OR "solution focused therapeutic"[All Fields] OR "solution focused therapeutics"[All Fields] OR "solution focused therapeutical"[All Fields]OR "solution-focussed therapies"[All Fields] OR "solution-focussed therapy"[All Fields] OR "solution-focussed therapeutic"[All Fields] OR "solution-focussed therapeutics"[All Fields] OR "solution-focussed therapeutical"[All Fields]OR "solution focussed therapies"[All Fields] OR "solution focussed therapy"[All Fields] OR "solution focussed therapeutic"[All Fields] OR "solution focussed therapeutics"[All Fields] OR "solution focused therapeutical"[All Fields] OR "self-control therapies"[All Fields] OR "self-control therapy"[All Fields] OR "self-control therapeutics"[All Fields] OR "self-control therapeutical"[All Fields] OR "self-control therapeutic"[All Fields] OR "self-control training"[All Fields] OR "self-control trainings"[All Fields] OR "self control therapies"[All Fields] OR "self control therapy"[All Fields] OR "self control therapeutics"[All Fields] OR "self control therapeutical"[All Fields] OR "self control therapeutic"[All Fields] OR "self control training"[All Fields] OR "self control trainings"[All Fields] OR "systemic therapies"[All Fields] OR “dialectical behavior therapy"[All Fields] OR "dialectical therapeutics"[All Fields] OR "dialectical therapeutic"[All Fields] OR "dialectical therapeutical"[All Fields] OR "dialectical therapeutist"[All Fields] OR "dialectical therapeutists"[All Fields] OR "systemic therapy"[All Fields] OR "systemic therapeutics"[All Fields] OR "systemic therapeutical"[All Fields] OR "systemic therapeutic"[All Fields] OR "systemic training"[All Fields] OR "systemic trainings"[All Fields] OR "family-based therapies"[All Fields] OR "family-based therapy"[All Fields] OR "family-based therapeutics"[All Fields] OR "family-based therapeutical"[All Fields] OR "family-based therapeutic"[All Fields] OR "family-based training"[All Fields] OR "family-based trainings"[All Fields] OR “Nutritional counseling”[All Fields] OR “Nutritional rehabilitation”[All Fields] Pharmacotherapy [MH] OR "medication"[MH] OR "drug therapy"[All Fields] OR "polypharmacy"[All Fields] OR "nutrition therapy"[All Fields] “hormonal therapy” [All Fields])

3. Effectiveness (outcome)

(“Treatment outcome"[mesh] OR "outcome"[tiab] OR effectiv*[tiab] OR "efficacy"[tiab])

4. RCT filter

(randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized controlled trials [mh] OR random allocation [mh] OR double-blind method [mh] OR single-blind method [mh] OR clinical trial [pt] OR clinical trials [mh] OR "clinical trial" [tw] OR ((singl* [tw] OR doubl* [tw] OR trebl* [tw] OR tripl* [tw]) AND (mask* [tw] OR blind* [tw])) OR "latin square" [tw] OR placebos [mh] OR placebo* [tw] OR random* [tw] OR research design [mh:noexp] OR comparative study [pt] OR evaluation studies [pt] OR follow-up studies [mh] OR prospective studies [mh] OR cross-over studies [mh] OR control[tw] OR controll*[tw] OR prospectiv* [tw] OR volunteer* [tw]) NOT (animal [mh] NOT human [mh]

Selected characteristics of the studies comparing psychological treatment with control treatment in patients with anorexia nervosa

First author, Year	Intervention (*n*)	Format; setting	Sessions (*n*)	Training; manual	Target group	Baselineweight	Onset age	Duration of illness (years/months)	Definition of anorexia nervosa	Weight measures	Eating disorder measures	Quality of life measures	Risk of bias
Byrne, 2017	MANTRA (41)	Individual; OP	25-40	Yes; N.M.	Adults	16.9 (BMI)	N.M.	5y	DSM-IV-TR	BMI	EDE-I Global	CIA	0
	CBT-E (39)	Individual; OP	25-40	Yes; YES	Adults	16.6 (BMI)	N.M.	4y					
	SSCM (40)	Individual; OP	25-40	Yes; N.M.	Adults	16.6 (BMI)	N.M.	2y					
Dare, 2001	FPT[1] (21)	Individual; OP	25	Yes; N.M.	Adults	15.0 (BMI)	18.8	6.7y	DSM-IV	kg BMI %ABW	-	-	0
	FT (22)	Family; OP	14	N.M.; N.M.	Adults	15.2 (BMI)	20.5	5.8y					
	CAT (22)	Individual; OP	13	N.M.; N.M.	Adults	16.0 (BMI)	19.9	6.7y					
	Routine (19)	Individual; OP	11	N.M.; N.M.	Adults	15.3 (BMI)	16.6	6.1y					
Geist, 2000	FT (12)	Family; IP	8	N.M.; N.M.	Adolescents	41.1 (kg)	< 18	N.M.	DICA-R	% IBW	EDI-2	-	2
	FGP (13)	Family; IP	8	N.M.; N.M.	Adolescents	41.1 (kg)	< 18	N.M.					
Godart, 2012	TAU + FT (12)	Family; OP	34	N.M.; N.M.	Adolescents	17.0 (BMI)	14.7	16.6 m	DSM-IV	BMI	EDI	WSAS	1
	TAU (30)	Family and individual; OP	27	N.M.; N.M.	Adolescents	16.9 (BMI)	15.0	17.1 m					
Gowers, 2007	MI, CBT, Parental Feedback, DT (57)	Family and Individual; OP	N.M.	No; No	Adolescents	15.3 (BMI)	N.M.	13 m	DSM-IV	BMI % IBW	MROAS EDI-2	-	1
	CT + FT (56)	Family and individual; IP	26-30	Yes; Yes	Adolescents	15.3 (BMI)	N.M.	13 m					
	TAU (55)	Family and individual; OP	N.M.	N.M.; No	Adolescents	15.5 (BMI)	N.M.	13 m					
Hall, 1987	PT (15)	Family and individual; OP	12	Yes; N.M.	Adults & adolescents	41.0 (kg)	17.1	29.7 m	N.M.	kg & deviation below MPMW	MROAS	-	2
	DA (15)	Individual; OP	12	N.M.; N.M.	Adults & adolescents	39.5 (kg)	17.5	24.5 m					

(Continued)

First author, Year	Intervention (*n*)	Format; setting	Sessions (*n*)	Training; manual	Target group	Baselineweight	Onset age	Duration of illness (years/months)	Definition of anorexia nervosa	Weight measures	Eating disorder measures	Quality of life measures	Risk of bias
McIntosh, 2005	CBT (19)	Individual; OP	20	N.M.; Yes	Adults & adolescents	17.3 (BMI)	N.M.	N.M.	BMI < 17.5	kg BMI % Body fat	EDE EDI-2	GAF	2
	IPT (22)	Individual; OP	20	N.M.; Yes	Adults & adolescents	17.3 (BMI)	N.M.	N.M.					
	SSCM (16)	Individual; OP	20	N.M.; N.M.	Adults & adolescents	17.3 (BMI)	N.M.	N.M.					
Parling, 2016	ACT (24)	Individual; OP	19	No; Yes	Adults	17.5 (BMI)	14.8	N.M.	SCID-1-RV	BMI	EDE	QOLI	1
	TAU (19)	Individual; OP	N.M.	No; No	Adults	18.1 (BMI)	13.8	N.M.					
Pillay, 1981	SST (11)	Group; IP	12	N.M.; N.M.	Adults	41.0 (kg)	N.M.	N.M.	N.M.	kg % weight increase % MMPW % MMPW categories	-	SAD	2
	Placebo (12)	Group; IP	12	N.M.; N.M.	Adults	40.2 (kg)	N.M.	N.M.					
Russel, 1987	FT (10) sub 1	Family; OP	11	Yes; N.M.	Adolescents	65.9 (%ABW)	15.3	1.2y	N.M.	%ABW	MROAS	-	2
	FT (10) sub 2	Family; OP	11	Yes; N.M.	Adults	66.0 (%ABW)	14.3	5.9y					
	FT (10) sub 3	Family; OP	11	Yes; N.M.	Adults	63.1 (%ABW)	24.6	3.0y					
	TAU (27)	Individual; OP	16	Yes; N.M.	N.M.	N.M.	N.M.	N.M.					
Schmidt, 2012	MANTRA (34)	Individual; OP	20-30	Yes; Yes	Adults	16.3 (BMI)	19.1	77.3 m	DSM-IV & EDNOS BMI <18.5	BMI kg	EDE-I	CIA	0
	SSCM (37)	Individual; OP	20-30	Yes; Yes	Adults	16.4 (BMI)	18.7	83.5 m					
Schmidt, 2015	MANTRA (72)	Individual; OP	20-30	Yes; Yes	Adults	16.6 (BMI)	17.3	9.3y	DSM-IV & EDNOS BMI <18.5	BMI kg	EDE-I	CIA	0
	SSCM (70)	Individual; OP	20-30	Yes; Yes	Adults	16.6 (BMI)	18.1	7.2y					
Serfaty, 1999	CT (25)	Individual; OP	20	Yes; Yes	Adults & Adolescents	16.2 (BMI)	N.M.	5.0y	DSM-III-R	BMI	EDI	-	2
	DA (10)	Individual; OP	20	N.M.; N.M.	Adults & Adolescents	17.0 (BMI)	N.M.	2.2y					
Touyz, 2013	CBT (31)	Individual; OP	30	Yes; Yes	Adults	16.3 (BMI)	N.M.	17.7y	DSM-IV excl. amenorrhea criterion	kg BMI	EDE-I ANSOCQ	EDQOL SF012 MCS SF-12 PCS WSAS	0
	SSCM (32)	Individual; OP	30	Yes; Yes	Adults	16.1 (BMI)	N.M.	15.5y					
Treasure, 1995	CAT (14)	Individual; OP	20	N.M.; YES	Adults	15.6 (BMI)	20.8	N.M.	ICD-10	BMI kg M weight gain (kg)	MROAS	-	2
	EBT (16)	Individual; OP	20	N.M.; YES	Adults	15.0 (BMI)	20.4	N.M.					

(Continued)

First author, Year	Intervention (*n*)	Format; setting	Sessions (*n*)	Training; manual	Target group	Baselineweight	Onset age	Duration of illness (years/months)	Definition of anorexia nervosa	Weight measures	Eating disorder measures	Quality of life measures	Risk of bias
Wade, 2009	MI (22)	Individual; IP	4	Yes; Yes	Adults & adolescents	16.6 (BMI)	16.9	6.9y	BMI <19	-	EDE ANSOQ	-	2
	TAU (25)	N.M.; IP	N.M.	N.M.; N. M.	Adults & adolescents	16.1 (BMI)	16.5	3.2y					
Zipfel, 2014	FPT^2 (80)	Individual; OP	39.3	Yes; Yes	Adults	16.6 (BMI)	N.M.	N.M.	SCID I	BMI kg	EDI-e SIAB-EX	-	0
	CBT-E (80)	Individual; OP	44.8	Yes; Yes	Adults	16.8 (BMI)	N.M.	N.M.					
	TAU (82)	Individual; OP	N.M.	N.M.; N. M.	Adults	16.8 (BMI)	N.M.	N.M.					

ABW = Adjusted body weight; ACT = Acceptance and Commitment Therapy; ANSOCQ = Anorexia Stages of Change Questionnaire; BMI = Body Mass Index; BT = Behavior therapy; CAT = Cognitive Analytical Therapy; CBT = Cognitive Behavioral Therapy; CBT-E; Cognitive Behavior Therapy-Enhanced; CIA = Clinical Impairment Assessment; CT = Cognitive Therapy; DA = Dietary Advice; DICA-R = Diagnostic Interview for Children and Adolescents- revised; DSM = Diagnostic and Statistical Manual for Mental Disorders; DT = Dietary Therapy; EBT = Educational Behavioral Therapy; EDE = Eating Disorder Examination; EDI = Eating Disorder Inventory; EDQOL = Eating Disorders Quality of Life; FGP = Family group psychoeducation; FPT^1 = Focal psychoanalytic psychotherapy; FPT^2 = Focal psychodynamic therapy; FT = Family therapy; GAF = Global Assessment of Functioning score; IBW = Ideal body weight; ICD = International Statistical Classification of Diseases and Related Health Problems; IP = Inpatient setting; IPT = Interpersonal Therapy; IST = Individual Supportive Therapy; MANTRA = Maudsley Model of Anorexia Nervosa Treatment for Adults; MI = motivational interviewing; MPMW = Matched population mean weight; MROAS = Morgan-Russell Outcome Assessment Schedule; N.M. = not mentioned; OP = Outpatient setting; PT = Psychotherapy; QOLI = Quality of Life Inventory; RT = Routine treatment; SAD = Social Avoidance Distance Questionnaire; SCID = Structured Clinical Interview for DSM; SF-12 = Short form Health Status Questionnaire; SIAB-EX = Structured Interview for Anorectic and Bulimic disorders; SSCM = Specialist Supportive Clinical Management; SST = Social Skills Training; TAU = Treatment as usual; WSAS = Weissman's Social Adjustment Scale.

APPENDIX C

STUDIES INCLUDED IN META-ANALYSIS

Byrne, S., Wade, T., Hay, P., Touyz, S., Fairburn, C. G., Treasure, J., ... Crosby, R. D. (2017). A randomised controlled trial of three psychological treatments for anorexia nervosa. Psychological Medicine, *47*, 1-11. https://doi.org/10.1017/S0033291717001349

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